



Separation of m/p-Aminoacetophenone Using Hydrotrophy

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Abstract: The aqueous solubilities of m/p-aminoacetophenone in different concentrations (0-3.0 mol/L) of hydrotropes such as diethyl nicotinamide, sodium pseudocumene sulfonate and sodium thiocyanate solutions at different system temperatures (303K to 333K) were studied. The percentage extraction (%E) of m-aminoacetophenone from m/p-aminoacetophenone mixture increases with increase in hydrotrope concentration. A Minimum Hydrotrope Concentration (MHC) in the aqueous phase was required to initiate the significance of the %E of m-aminoacetophenone. Percentage extraction (%E) is the ratio of moles of m-aminoacetophenone extracted in presence and absence of a hydrotrope. The sensitivity and feasibility of the proposed process are examined by carrying out solubilization and equilibrium precipitation experiments with the mixtures of various compositions. The effectiveness of hydrotropes was measured in terms of Setschenow constant Ks. The extraction data are also fitted in a polynomial equation as the function of hydrotrope concentration. The solubilized material can be recovered by dilution with water.

Keywords: Hydrotropy, Solubilization, Enhanced solubility, Extraction.

Introduction

A range of industrial mixtures having close boiling point isomeric or non isomeric components present a challenging separation problem, as in most cases conventional separation methods cannot be successfully applied. These components usually have similar chemical properties and molecular sizes and comparable volatilities. A simple technique is employed which involves either solubilization and precipitation i.e., the solubilization of the mixture in a hydrotrope solution and subsequent selective precipitation of a desired component by controlled dilution with water.

Hydrotropy is a unique and unprecedented solubilization technique in which certain chemical components termed as hydrotropes can be used to affect a several fold increase in the solubility of sparingly soluble solutes under normal conditions¹⁻⁴.

Hydrotropic substances are a class of chemical compounds that are freely soluble in water. Hydrotropes are much effective at high concentrations which in turn enhance the aqueous solubility of organic compound, because of the possibility of molecular solution structures probably in the form of stack-type aggregates. The solubilised solute will therefore precipitate out on dilution with water from most hydrotropic solutions. This process may be used to recover the solute in a pure form, and the remaining mother liquor may be used to concentrate the hydrotrope for recycle⁵.

In recent years the aggregation behaviour of common hydrotropes by several techniques have been determined^{6,7}. The self aggregation of the hydrotropes has been considered to be a pre-requisite for a number of applications in various fields such as drug solubilization⁸⁻¹⁰, chemical reactions¹¹, separation of organic compounds¹² extraction of curcuminoids from turmeric¹³, piperine from *Piper nigrum*¹⁴ and boswellic acids from *Boswellia serrata* resins¹⁵. The present work was initiated for the fundamental study of the global role of hydrotropes in the selective separation of a component from mixtures via solubilization and precipitation techniques. With particular emphasis on both the theoretical understanding of the mechanistic behavior and the experimental studies which demonstrates the utility of hydrotropes in the separation of commercially important mixtures¹⁶⁻²¹. The system m/p-aminoacetophenone (molecular weight $M = 135.16$) was chosen, for enhancing its solubility using several commercially available hydrotropes. Since m-aminoacetophenone serves as a raw material/intermediate for a wide variety of chemical and petro products, and this makes its separation from any liquid mixture which has been difficult until now.

The separation of m/p-aminoacetophenone through solubilization and selective precipitation is important as both these isomers have not only close boiling points but also close melting points. The melting points of m/p-aminoacetophenone are 99 and 106°C, while the boiling points are 290 and 294°C, respectively. All hydrotropes are non- reactive, non-toxic and do not produce any change in temperature effect when dissolved in water. The cheapness and easy availability are other factors considered in the selection of hydrotropes.

Experimental

Materials

All the chemicals used in this work were manufactured by the Loba Chemie Pvt. Ltd., Mumbai. with a manufacturer's stated purity of 99.9 %. The hydrotropes used in this work viz., diethyl nicotinamide, sodium pseudocumene sulfonate and sodium thiocyanate are of analar grade. Double distilled water was used for the preparation of hydrotropic solutions.

Methods

The experimental setup for conducting a single-stage batch wise liquid-liquid extraction consisted of a thermostatic bath and a separating funnel. Measurement of the solubility of m-amino acetophenone was carried out at temperatures of 303, 313, 323, and 333 K. For each solubility test, an equal volume (100mL) of m/p- aminoacetophenone was thoroughly mixed to make a single-phase solution using a mechanical shaker. The hydrotrope solutions of different known concentrations were prepared by dilution with distilled water. Following to this, 100 ml of m/p- amino acetophenone mixture was taken and added to 100ml of hydrotrope solution of known concentration. The mixture was then made to mix continuously for three hours. The mixture was then allowed to settle and was transferred to a separating funnel, which was immersed in a thermostatic bath with a temperature controller within $\pm 0.1^\circ\text{C}$. The setup was kept overnight for equilibration. After equilibrium was attained, the organic phase containing m-amino acetophenone was carefully separated and analyzed to determine the concentration using a high-performance liquid chromatography (HPLC). All the solubility experiments were conducted in duplicate runs to check their

reproducibility. The %E has been calculated from these solubility data. The observed error was <2%.

Results and Discussion

Extracted m- amino acetophenone been shown in schematic comparative HPLC chromatogram in Fig.1.

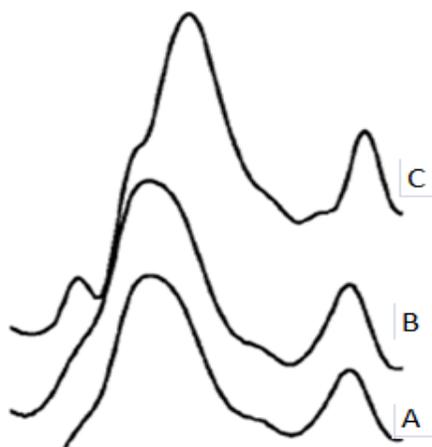


Figure 1. Comparative HPLC chromatogram **A.** diethylnicotinamide; **B.** sodium pseudocumene sulfonate; **C.** sodium thiocyanate.

Experimental data on the effect of hydrotropes, i.e., diethyl nicotinamide, sodium pseudocumene sulfonate and sodium thiocyanate on the percentage extractions (%E) of m- aminoacetophenone are presented in the form of polynomial fit in Figs. 2–4, and solubility of m- aminoacetophenone are shown in Figs. 5–7. Percentage extraction (%E)) is the ratio of extraction of m-aminoacetophenone in the presence and absence of hydrotrope, respectively.

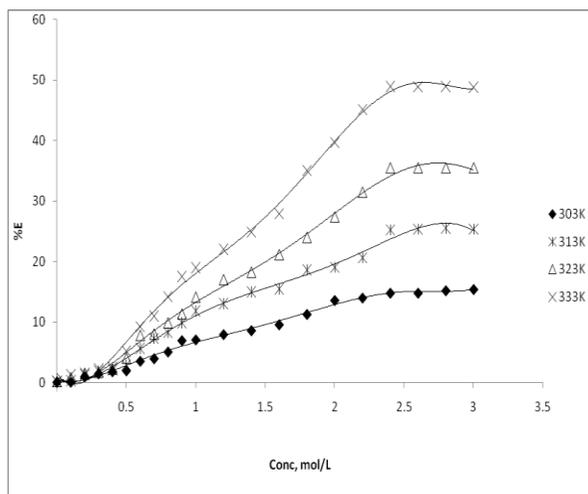


Figure 2. Effect of diethylnicotinamide concentration (C) on percentage extraction (%E) of m-aminoacetophenone

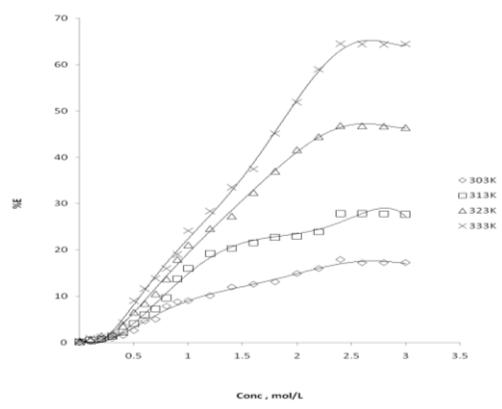


Figure 3. Effect of sodium pseudocumene sulfonate concentration (C) on percentage extraction(%E) of m-aminoacetophenone.

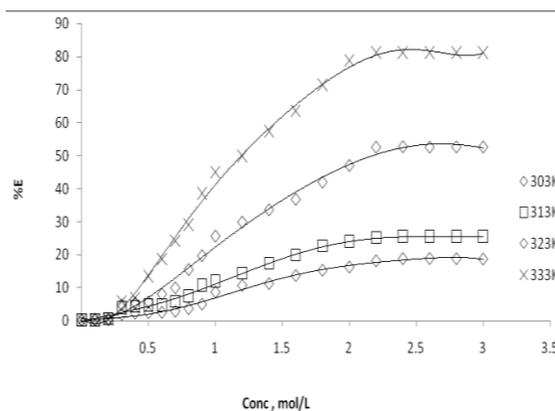


Figure 4. Effect of sodium thiocyanate concentration (C) on percentage extraction (%E) of m-aminoacetophenone.

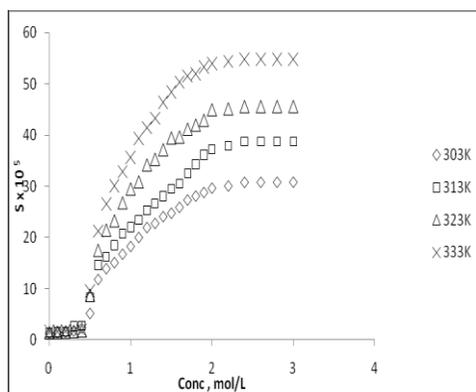


Figure 5. Effect of diethylnicotinamide concentration (C) on solubility of m-aminoacetophenone.

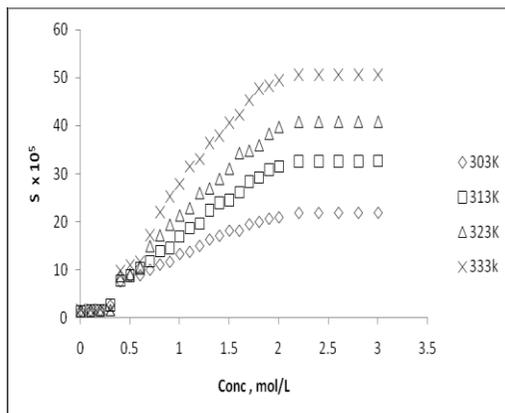


Figure 6. Effect of sodium pseudocumene sulfonate concentration (C) on solubility of m-aminoacetophenone.

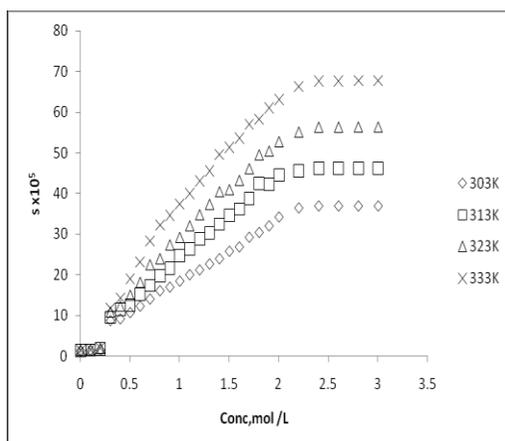


Figure 7. Effect of sodium thiocyanate concentration (C) on solubility of m-aminoacetophenone.

Sodium thio cyanate is one of the hydrotropes used in this study. It was observed that the %E of m-aminoacetophenone did not show any appreciable increase until 0.20 mol/L of sodium thiocyanate, however, upon subsequent increase in the concentration of sodium thiocyanate, i.e., 0.30 mol/L, the %E of m-aminoacetophenone was found to increase significantly. This concentration of sodium thiocyanate in the aqueous phase, i.e., 0.30 mol/L, is termed as the Minimum Hydrotrope Concentration (MHC), which is the minimum required amount of sodium thiocyanate in the aqueous phase to initiate significant increase in the percentage extraction of m-aminoacetophenone. It was observed that the MHC of sodium thiocyanate in the aqueous phase does not vary even at increased system temperatures, i.e., 313, 323, and 333 K.

A similar trend in the MHC requirement has also been observed for other hydrotropes. Therefore, it is evident that hydrotropic separation is displayed only above the MHC, irrespective of the system temperature. Hydrotrope does not seem to be operative below the MHC, which may be a characteristic of a particular hydrotropes with respect to each solute.

The percentage extraction effect varies with concentration of the hydrotropes. In this case, a clear increasing trend in the percentage extraction of m- aminoacetophenone was observed above the MHC of sodium thiocyanate. This increase is maintained only up to a certain concentration of sodium thiocyanate in the aqueous phase, i.e, 2.20 mol/L beyond which there is no appreciable increase in the percentage extraction of m- aminoacetophenone. This concentration of sodium thiocyanate in the aqueous phase is referred to as the maximum hydrotrope concentration (C_{max}). From the analysis of the experimental data, it is observed that further increase in the hydrotrope concentration beyond C_{max} does not cause any appreciable increase in the percentage extraction even up to 3.0 mol/L in the aqueous phase. Similar to the MHC values, the C_{max} values of the hydrotropes also remained unaltered with the increase in system temperature. (Table 1) The maximum Effectiveness of hydrotrope (ϕ) which is the ratio of the percentage extraction value in the presence and absence of a hydrotrope, respectively was determined and the highest value of (ϕ) 63.76 case of sodium thiocyanate at a system temperature of 333 K (Table 2).

Table 1. MHC and C_{max} values of hydrotropes.

S.No	Hydrotropes	MHC, mol/L	Cmax , mol/L
1	diethylnicotinamide	0.5	2.4
2	sodium pseudocumene sulfonate	0.4	2.4
3	sodium thiocyanate	0.3	2.2

Table 2. Effectiveness of hydrotrop (ϕ).

S.No	Hydrotropes	303K	313K	323K	333K
1	diethylnicotinamide	14.78	25.25	35.44	48.96
2	sodium pseudocumene sulfonate	17.88	27.87	46.86	60.24
3	sodium thiocyanate	18.22	23.14	52.53	63.76

Effectiveness of Hydrotrope

The effectiveness factor for each hydrotrope with respect to the percentage extraction of m-aminopropiophenone at different system temperatures was determined by applying the model suggested by Setschenow and later modified by Phatak and Gaikar as given by the equation:

$$\log (E/E_m) = K_s(C_s - C_m), \quad (1)$$

where E and E_m is the %E values of m- aminoacetophenone maximum hydrotrope concentration C_s (same as C_{max}) and the minimum hydrotrope concentration C_m (same as MHC) respectively. The Setschenow constant (K_s) can be considered as a measure of the effectiveness of a hydrotrope at any given conditions of hydrotrope concentration and system temperature. The Setschenow constant values of hydrotropes, namely, diethyl nicotinamide, sodium pseudo cumene sulfonate and sodium thiocyanate for percentage extractions of m- aminoacetophenone different system temperatures are listed in Table. 3. The highest value was observed as 1.042 in the case of sodium thiocyanate as the hydrotrope at temperature 333K.

Table 3. Setschenow constant [K_s] values of hydrotropes with respect to m-aminoacetophenone.

S.No	Hydrotropes	303K	313K	323K	333K
1	diethylnicotinamide	0.582	0.713	0.788	0.864
2	sodium pseudocumene sulfonate	0.606	0.705	0.818	0.889
3	sodium thiocyanate	0.675	0.736	0.933	1.042

Since the exponential relation may not be valid at lower and higher hydrotrope concentrations, the data have been fitted in a polynomial equation of the form

$$Y = A C_s^6 + B C_s^5 + C C_s^4 + D C_s^3 + E C_s^2 + F C_s + G \text{ ----- } 2$$

which give a better fit for the solubility data. The values of correlation constants "A-G" are reported in Table 4 to 6. The solid curves in Figs.2-4 are from these polynomial equations.

Correlation Constants for Polynomial Equation

Table 4. Effect of the diethyl nicotinamide.

Temp, K	A	B	C	D	E	F	G
303	0.905	-8.48	-29.97	-50.1	39.5	-5.54	0.37
313	0.13	-3.22	19.28	-47.2	49.88	-8.29	0.544
323	1.34	-13.81	53.14	-95.99	82.74	-15.1	0.908
333	3.26	-31.13	111.7	-188.2	151.3	-30.44	1.54

Table 5. Effect of the sodium pseudo cumene sulfonate.

Temp,K	A	B	C	D	E	F	G
303	0.91	-9.571	38.48	-73.48	65.22	-13.19	0.63
313	1.11	7.13	-10.32	-16.3	45.83	11.09	0.77
323	1.61	-5.48	57.31	-104.8	97.32	-17.55	0.94
333	3.42	-32.35	114.6	-190.9	154.1	-27.53	1.08

Table 6. Effect of the sodium thiocyanate.

Temp,K	A	B	C	D	E	F	G
303	-0.77	3.81	-15.22	24.28	-12.28	11.21	-0.26
313	-0.34	3.81	-15.22	24.28	-12.28	1.21	-0.26
323	0.59	-6.39	27.51	-62.86	75.24	-12.73	0.85
333	3.49	-33.46	125.4	-235	218.1	-38.42	1.12

Conclusions

Selective solubilization of isomeric mixtures of m/p- aminoacetophenone were determined in aqueous solutions of several hydrotropes at different hydrotrope concentrations and temperatures. The MHC and C_{max} values of hydrotropes with respect to m-aminoacetophenone can be used for the recovery of the dissolved m-aminoacetophenone and hydrotrope solutions at any hydrotrope concentration between MHC and C_{max} by simple dilution with distilled water. It was possible to extract 81% of the material and the process was optimized with respect to concentration of hydrotrope solution, and temperature required for the extraction of m-aminoacetophenone. From the data obtained by this study, it is found that hydrotrope concentration gives self-aggregation at higher minimum concentration. These sigmoidal-type solubility variations are influenced by molecular structures. The differences in solubilities with hydrotrope concentration and temperature can be employed for the separation of closely related compounds. This will eliminate the huge cost and energy normally involved in the separation of solubilised m-aminoacetophenone from its solution. Hence sodium thiocyanate is found to be the best suitable hydrotrope for the enhancement of solubility of poorly soluble m-aminoacetophenone within the framework of the present investigation.

Notation

C [mol/L]: Concentration of hydrotrope

C_{max} [mol/L]: Maximum hydrotrope concentration

C_s [mol/L]: Maximum hydrotrope concentration

K_s [-]: Setschenow constant

E [-]: %E of m-aminoacetophenone at any hydrotrope concentration

E_m [-]: %E of m-aminoacetophenone at maximum hydrotrope Concentration

C_m [mol/L]: Minimum hydrotrope concentration

MHC [mol/L]: Minimum hydrotrope concentration

T [K]: Temperature

Φ [-]: Maximum enhancement factor.

References

1. Badwan, A.-A. El-Khordagui, L.-K., and Saleh, A.-M. *Int.J. Pharma*, 1983 ,**13**: 67-74.
2. Janakiraman, B.; Sharma, M. M. "Chem. Engg and science. 1985, 40, 2156-2158.
3. Saleh, A.-M. and El-Khordagui, L.-K. "Int.J. Pharma, 1985,24: 231- 238.
4. Balasubramanian, D., Srinivas, V., Gaikar, V.-G., and Sharma, M. -M. *J. Phy Chem*, 1989,93: 3865-3870.
5. Neuberg .c, *Biochem. Z.*, 76, 107 1916.
6. Agarwal, M. and Gaikar, V.-G. *Sep.Tech*, 1992, 2: 79-84.
7. Liaonanchen, X. and Micheau, J.-C *J.Coll and Int. Sci*, 2002, 249: 172-179.
8. Lee, J., Lee, S. C., Acharya, G., Chang, C. and Park, K: *Pharm. Res.*, 2003; 20(7): 1022-1030

9. Maheshwari.R.K, Deswal.s, Tiwari.D, Ali.N, and Jain.S, Asian J. Chem. 2008,20,(1), 805-807.
10. Maheshwari.R.K, Asian J. Chem, 2006, 18,(1), 393-396.
11. Khadilkar B.M, Gaikar V. G and Chitnavis. A. A.; Tetrahedron Lett. 1995, 36(44): 8083-8086.
12. Gaikar. V. G. and Phatak. P. V, Sep. Sci. Tech., 1999, 34,(3), 439-459.
13. Dandekar. D. V. and Gaikar. V. G Sep. Sci. Technol., 2003, 38, (5)1185-1215.
14. Raman.G and Gaikar,V.G; Ind. Eng.Chem. Res., 2002; 41(12): 2966-2976.
15. Raman.G and Gaikar,V.G, Langmuir, 2003 19, (19)8026-8032.
16. Nagendra Gandhi. N and Dharmendra Kumar. M. "J. Chem. Eng. Data 2000, 45, 419–423.
17. Nagendra Gandhi.N , Dharmendra Kumar.M, and N Sathyamurthy.N , "J. Chem. Eng. Data. 1998,43: 695-699.
18. Nagendra Gandhi .N, Dharmendra Kumar. M and Sathyamurthy.N. H. J.ind.chem, 1998, 26, 63-68.
19. Nagendra Gandhi.N and Dharmendra Kumar.M, Bioprocess Eng, 2000, 449:0116.
20. Meyyappan.N and Nagendra Gandhi N. J. Chem. Eng. Data, 2004, 49 (5), 1290–1294.
21. Meyyappan. N and Nagendra Gandhi, N. J. Chem. Eng. Data, 2005, 50, 796—800.



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